-- This application is a divisional of U.S.S.N. 09/218,950, filed December 22, 1998, now U.S. Patent No. 6,284,240 B1, which is a divisional of U.S.S.N. 08/284,391, filed August 2, 1994, now U.S. Patent No. 5,851,828, which is a continuation-in-part of U.S.S.N. 08/195,395, filed February 14, 1994, now abandoned, which is a continuation-in-part of U.S.S.N. 07/847,566, filed March 6, 1992, now abandoned, which is a continuation-in-part of U.S.S.N. 07/665,961, filed March 7, 1991, now abandoned.--

A1 cont

Replace the third full paragraph on page 21 with the following paragraph rewritten in clean form:

--**FIG. 1A** presents the amino acid sequence about the site of fusion between CD4 (residues 1-369) and different receptor chains (SEQ ID NOS: 38-41). The underlined sequence shows the position of the amino acids encoded within the BamHI site used for fusion construction. The beginning of the transmembrane domain is marked with a vertical bar. The η sequence is identical to the ζ sequence at the amino terminus, but diverges at the carboxyl terminus (Jin et al., Proc. Natl. Acad. Sci. USA 87:3319-3323 (1990)). **FIG. 1B** presents flow cytometric analysis of surface expression of CD4, CD4:ζ, CD4:γ and CD4:η in CV1 cells. Cells were infected with virus expressing CD4 chimeras or $CD16_{PI}$, incubated for 9 hours at 37°C, and stained with phycoerythrin-conjugated anti-CD4 MAb Leu3A.--

A2

Replace the first full paragraph on page 24 with the following paragraph rewritten in clean form:

--**FIG. 7A-B** shows characterization of the CD16:ζ chimeric receptor. **FIG. 7A** is a schematic diagram of the CD16:ζ fusion protein. The extracellular portion of the phosphatidylinositol-linked form of monomeric CD16 was joined to dimeric ζ just external to the transmembrane domain. The protein sequence at the fusion junction is shown at the bottom (SEQ ID NOS: 42, 43). **FIG. 7B** shows a flow cytometric analysis of calcium mobilization following crosslinking of the CD16:ζ chimera in either a TCR positive or TCR negative cell line. The mean ratio of violet to blue fluorescence (a measure of relative calcium ion concentration) among cell populations treated with antibodies at time 0 is shown. Solid squares, the response of Jurkat cells to anti-CD3 MAb OKT3; solid triangles, the response of CD16:ζ to anti-CD16 MAb 3G8 crosslinking in the REX33A TCR^- mutant; open squares, the response to CD16:ζ crosslinking in the Jurkat TCR^- mutant line JRT3.T3.5; open triangles, the response to CD16:ζ crosslinking in Jurkat cells; crosses, the response to nonchimeric CD16 in Jurkat cells; and dots, the response to nonchimeric CD16 in the REX33A TCR^- cell line.--

Replace the first full paragraph on page 25 with the following paragraph rewritten in clean form:

--**FIG. 9A-D** shows that elimination of the potential for transmembrane

interactions reveals a short ζ segment capable of mediating cytolysis. **FIG. 9A** is a schematic diagram of the monomeric bipartite and tripartite chimeras. At the top is the CD16:ζ construct truncated at residue 65 and lacking transmembrane Cys and Asp residues. Below are the CD16:CD5:ζ and CD16:CD7:ζ constructs and related controls. The peptide sequences of the intracellular domains are shown below (SEQ ID NOS: 45-47). **FIG. 9B** shows the cytolytic activity of monomeric chimera deletion mutants. The cytolytic activity of cells expressing CD16:ζ (solid circles; mfi 495) was compared to that of cells expressing CD16:ζAsp66* (solid squares; mfi 527) or the mutants CD16:ζCys11Gly/Asp15Gly/Asp66*, (open squares; mfi 338) and CD16:ζCys11Gly/Asp15Gly/Glu60* (filled triangles; mfi 259). **FIG. 9C** shows the cytolytic activity mediated by tripartite--

Replace the first full paragraph on page 27 with the following paragraph rewritten in clean form:

--**FIG. 11A-B** shows alignment of internal repeats of ζ and comparison of their ability to support cytolysis. **FIG. 11A** is a schematic diagram of chimeras formed by dividing the ζ intracellular domain into thirds and appending them to the transmembrane domain of a CD16:7 chimera. The sequences of the intracellular domains are shown below (SEQ ID NOS: 48-50), with shared residues boxed, and related residues denoted by asterisks. **FIG. 11B** shows the cytolytic potency of the three ζ subdomains. Solid

circles, cells expressing CD16:ζ (mfi 476); solid squares, CD16:7:ζ(33-65) (mfi 68); open squares, CD16:7:ζ(71-104) (mfi 114); and solid triangles, CD16:7:ζ(104-138) (mfi 104).--

Replace the first full paragraph on page 28 with the following paragraph rewritten in clean form:

--**FIG. 15A-E** shows identification of residues in the FcRγII A tail (SEQ ID NO: 53) which are important for cytolysis. **FIG. 15A** is a schematic diagram of the deletion constructs. **FIGS. 15B** and **15C** shows calcium mobilization and cytolysis by carboxyl-terminal deletion variants of CD16:FcRγII A. **FIGS. 15D** and **15E** show calcium mobilization and cytolysis by tripartite chimeras bearing progressively less of the amino terminus of the intracellular tail of CD16:FcRγII A.--

Replace full paragraphs 1-6 on page 31 with the following paragraphs rewritten in clean form:

--**FIG. 23** shows the nucleic acid (SEQ ID NO: 28) and amino acid (SEQ ID NO: 29) sequence of the D1-D4 domains of CD4 (CD4 Bam).

FIG. 24 shows the nucleic acid (SEQ ID NO: 30) and amino acid (SEQ ID NO: 31) sequence of the D1-D2 domains of CD4 (CD4 Nhe).

FIG. 25 shows the nucleic acid (SEQ ID NO: 32) and amino acid (SEQ ID NO:

33) sequence of the hinge, CH2, and CH3 domains of human IgG1 (Igh23 Bam).

FIG. 26 shows the nucleic acid (SEQ ID NO: 34) and amino acid (SEQ ID NO: 35) sequence of the transmembrane domain of CD7 (TM7 Bam Mlu).

FIG. 27 shows the nucleic acid (SEQ ID NO: 36) and amino acid (SEQ ID NO: 37) sequence of the intracellular domain of zeta (Zeta Mlu Not).

FIG. 28 shows the DNA sequence (SEQ ID NO: 51) and primary amino acid sequence (SEQ ID NO: 52) of a synthetic alpha helix.--

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Replace the first full paragraph on page 41 with the following paragraph rewritten in clean form:

--To identify the minimal ζ sequences necessary for cytolysis, a series of deletion mutants were prepared in which successively more of the ζ intracellular domain (SEQ ID NO: 44) was removed from the carboxyl terminus (Fig. 8A). Most of the intracellular domain of zeta could be removed with little consequence for cytolytic potential; the full length chimera CD16:ζ was essentially equal in efficacy to the chimera deleted to residue 65, CD16:ζAsp66* (Fig. 8B). A substantial decrease in cytotoxicity was observed on deletion to ζ residue 59 (chimera CD16:ζGlu60*), and further deletion to residue 50 resulted in slightly less activity. However complete loss of activity was not observed even when the intracellular domain was reduced to a three residue transmembrane anchor (Fig. 8B).--

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